

RECEIVED
CENTRAL FAX CENTER

NOV 27 2006

Appl. No. 10/658,823
Amdt. dated November 27, 2006
Reply to Office Action of July 25, 2006

PATENTREMARKS

Upon entry of the present amendment, claims 36-51 will be pending in the above-referenced patent application and are currently under examination. Claim 47 has been canceled. Claims 41, 42, 45, 46 and 48 are directed to non-elected species and have been withdrawn by the Examiner. Applicants note that if a generic claim is found allowable, the withdrawn claims should rejoined. Reconsideration of the application is respectfully requested.

Claim 51 has been added to provide that the hydrophobic, non-carbohydrate test compound:

comprises a member selected from the group consisting of a heteroaryl moiety having from 5 to 16 ring members wherein from 1 to 3 ring members are each independently selected from the group consisting of N, O and S wherein the heteroaryl ring structure is optionally substituted, and an aliphatic ring structure having from 3 to 7 ring members and is optionally substituted.

New claim 51 finds support throughout the specification. Specific support can be found in canceled claim 47 and pending claim 49. Additional support can be found in the specification in paragraphs [0012], [0038] and [0058] where the non-carbohydrate test compound is a heteroaryl moiety or an aliphatic ring structure. Support for the heteroaryl ring moiety can be found in paragraphs [0023] and [0024]. Support for the aliphatic ring structures can be found in paragraph [0020].

The claims are rejected under 35 U.S.C. § 103(a). Each of these rejections is addressed below in the order set forth by the Examiner.

Rejections under 35 U.S.C. § 103(a)

Claims 36-40, 43, 44, 47, 49 and 50 have been rejected under 35 USC § 103(a) as allegedly being obvious over Qiao *et al.* in view of Rabina *et al.*, Sousa *et al.* and Chung *et al.* Applicants respectfully traverse the rejection in view of the comments below.

A claim is considered obvious "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to

Appl. No. 10/658,823
Amdt. dated November 27, 2006
Reply to Office Action of July 25, 2006

PATENT

which said subject matter pertains" (35 USC § 103(a)). Several elements are necessary in order to make a *prima facie* case of obviousness (MPEP § 2143):

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

In order for the claims of the instant application to be obvious in view of the cited art, each reference must (1) provide some suggestion or motivation to modify the reference in order to teach all of the claim elements; (2) provide a reasonable expectation of success of making a compound of the instant application; and (3) teach or suggest all of the claim elements. As discussed in detail below, none of the cited references separately nor in combination, satisfies all three requirements under MPEP § 2143.

The Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of Qiao *et al.* to identify an inhibitor of a fucosyltransferase with a fluorescent labeled substrate and a hydrophobic test compound with aromatic ring structure, because Qiao *et al.* teaches the importance of fucosyltransferase inhibitors in the inflammatory process and tumor development and Rabina *et al.* teaches an immunofluorometric method for measurement of fucosyltransferase activity.

Qiao *et al.* teaches aza sugars as inhibitors of human α -1,3-fucosyltransferase V (Qiao *et al.*, p.7654, second column, first full paragraph). As the Examiner acknowledges, Qiao *et al.* does not teach a non-carbohydrate test compound, the use of an antibody to determine fucosyltransferase activity in an ELISA format, expression of fucosyltransferase in recombinant cell and the labeling of donor or acceptor substrate with fluorescent.

The Examiner cites Rabina *et al.* for the missing teaching of an immunofluorometric method for measurement of fucosyltransferase activity. However, Rabina *et al.* does not provide a teaching or suggestion of all the deficiencies of Qiao *et al.*, such as a non-carbohydrate inhibitor of glycosyltransferase. Thus, Rabina *et al.* provides neither suggestion or motivation to modify Qiao *et al.* in order to teach all of the elements of the instant claims.

Appl. No. 10/658,823
 Amdt. dated November 27, 2006
 Reply to Office Action of July 25, 2006

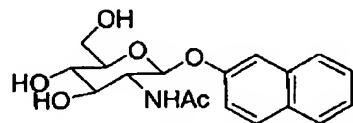
PATENT

The Examiner alleges that Sousa *et al.* teaches that hydrophobic amino acids in the active site of glucosyltransferase forms part of the recognition mechanism for the enzyme activity (Office Action page 4, citing Abstract of Sousa *et al.*). Applicants note, however, that the hydrophobic amino acids to which the Examiner refers are actually present on the **glycoprotein substrate**, and **not** on the glucosyltransferase, as stated by the Examiner (see Sousa *et al.* p.611 last paragraph to page 615, first column, last paragraph).

Sousa *et al.* elucidates the mechanism for quality control of protein folding in eukaryotic cells where only properly folded species are transported to the Golgi apparatus (Abstract). When the glycoprotein substrates unfold, hydrophobic portions of the glycoprotein substrate are revealed that remain hidden in the interior when folded. The glucosyltransferase described by Sousa *et al.* detects hydrophobic portions of the unfolded glycoprotein substrate in the vicinity of the oligosaccharide to which the enzyme adds a glucose (page 614, second column, last paragraph). There is nothing in the teachings of Sousa *et al.* that indicates the hydrophobic residues of the glycoprotein interact with the active site of the glucosyltransferase. Thus, there is no teaching in Sousa *et al.* of hydrophobic interactions are in any way associated with enzymatic activity of the glucosyltransferase studied there.

Accordingly, Sousa *et al.*, by itself or in any combination with Qiao *et al.* and Rabina *et al.*, does not teach or disclose the a method of identifying a hydrophobic, non-carbohydrate test compound that inhibits glucosyltransferase.

The Examiner further alleges that Chung *et al.* teaches the development of inhibitors based on the proposed active site model of the enzyme. However, the inhibitors taught by Chung *et al.* are limited to mixed aryl-carbohydrate compounds that are exemplified by compound 1a:



All of the compounds disclosed in Chung *et al.* include a carbohydrate moiety (see also compounds 1b, 1c and 2-9). None of the compounds in Chung *et al.* teach a heteroaryl moiety or an aliphatic ring structure *without* a carbohydrate moiety. Accordingly, Chung *et al.* provides no

Appl. No. 10/658,823
Amdt. dated November 27, 2006
Reply to Office Action of July 25, 2006

PATENT

suggestion or motivation that non-carbohydrate compounds can be used as inhibitors of glycosyltransferase.

In stark contrast to the teachings of the cited references, the claims of the instant application are drawn to a method of identifying an inhibitor of a glycosyltransferase where the inhibitor is a "hydrophobic, *non-carbohydrate* test compound." As explained above, only carbohydrate-containing compounds are taught in the cited references. Thus, none of the references either by themselves or in any combination, teach or suggest all the claim limitations of the instant application. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

RECEIVED
CENTRAL FAX CENTER

NOV 27 2006

Appl. No. 10/658,823
Amdt. dated November 27, 2006
Reply to Office Action of July 25, 2006

PATENT

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 415-576-0200.

Respectfully submitted,



Alexander Trimble
Reg. No. 52,301

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
Attachments
KLB:art
60920808 v1